

Application Ser. No.: 10/808,889  
Filing Date: March 25, 2004  
Examiner: Lee, Susannah E.

#### Remarks

In the Office Action, the Examiner noted that claims 1 to 18 are pending in the application; claim 18 is withdrawn from consideration; claims 1 to 5 are rejected; and that claims 6-17 are objected to. By this amendment, claims 1, 3, 4, 6, 8, 10-12, 14, 15 and 18 have been amended, and claim 5 has been cancelled without prejudice or disclaimer of the subject matter contained therein. Thus, claims 1-4 and 6-18 are pending in the application.

No new subject matter has been inserted through these amendments. All of the amendments are fully supported by the specification. Specifically, a few of the typographical and obvious translation errors have been corrected in the specification. Although most of the amendments are self-explanatory, specific amendments made are as set forth below.

The full paragraph on page 1, lines 19-27, has been amended to correct a minor typographical error, "CDKS" has been amended to read correctly as "CDKs". Also, the paragraph beginning at line 28, page 1 has been amended to correct the misspelled word, "esophageal," and to insert "of" between the word point and mutation. The paragraph on page 2, lines 30-34 has been amended to correct certain translation errors – the term "sulfonoester" has been amended to read correctly as "sulfonic acid ester" and the phrase "sulfonesters derivatives of those carbamates" has been amended to read more appropriately as "carbamates of those sulfonic acid ester derivatives." Another translation error has also been corrected in paragraph 5, lines 7-13 wherein various heteroaryl groups have been renamed properly to conform to the US practice, and a couple of typographical errors have also been corrected. Finally, the paragraphs at page 4, lines 22-27, and page 5, lines 14-17, have been amended to correct certain typographical errors as noted.

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Claims 1, 3 and 4 have been amended to delete unelected subject matter. For instance, definition of A is limited to aryl. Within the definition of R<sub>1</sub>, alkyl, alkoxy, aryl or heteroaryl, halogen and SO<sub>2</sub>Me have been deleted. Also, within the definition of R<sub>1</sub>, the definition of heterocyclyl has been limited to substituted or unsubstituted tetrahydrofuranyl, tetrahydropyranyl, pyrrolidinyl, 2-oxo-pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl or azepanyl. Support for this can be found in the specification at page 5, lines 12 and 13 where a much broader definition of heterocyclyl is provided. Further support for the limited definition as provided in amended claim 1 can be found at various places of the specification, more specifically, at Examples 18, 54, 56, 59, 60g, 60j, 60k, 60n, 60u, 60ae, 60aw, 60bd, 60bm, 60bn, 6-ca, 60cj, 60cy, 60dk and 60fj.

Similarly, within the definition of R<sub>2</sub>, various unelected subject matter, such as heteroalkyl, heterocyclylamino, heteroarylamino, heteroaryl, heterocycloalkyl, etc. have been deleted. However, when R<sub>2</sub> is -CO-amino, -CO-NHR<sub>3</sub>, -CO-NR<sub>3</sub>R<sub>4</sub>, also includes heterocyclyl selected from pyrrolidinylalkyl, 2-oxo-pyrrolidinylalkyl, piperidinylalkyl, tetrahydropyranylalkyl or morpholinylalkyl, alkylheterocycloalkyl selected from 4-alkylpiperazinylalkyl or N-alkyl-pyrrolidinylalkyl, and includes a limitation when R<sub>3</sub> and R<sub>4</sub> are taken together to form an alkylene chain optionally containing one to 4 heteroatoms "selected from azetidine, pyrrolidine or piperidine". Support for both of these can again be found at various places of the specification, broadly, at page 5, lines 14 and 15. Specific support can be found for either R<sub>3</sub> or R<sub>4</sub> as heterocyclyl at Examples 57k, 58k, 58u, 58v, 58ac, 58ag, 58ah, 58ai, 58aj, 59f, 59g, 59h, 59i, 59m, 59p and 59r; and for R<sub>3</sub> and R<sub>4</sub> taken together forming a heterocyclyl at Examples 58i, 58q, 58r, 58t and 58ac. Also, when R<sub>2</sub> is aryl or aralkyl, claim 1 as amended includes optional substituents to be heterocyclyl selected only from morpholinyl or alkyl piperazinyl and the heteroaryl is limited to oxadiazolyl. Again, support for this can be found at many places in the specification, specifically, at Examples 70b, 70h and 76a.

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Dependent claims 3, 4, 10 and 15 have similarly been amended so as to properly depend on claim 1. Since claim 5 has been canceled, dependence of claims 6, 8, 12 and 15 have been amended to depend upon claim 4. Claims 11 and 14 have been amended to delete compounds which are no longer within the scope of claim 1. Claim 15 has also been amended to correct a typographical error – misspelled “fluroroalkyl” has been amended to correctly read as --fluoroalkyl.-- Finally, claim 18 has been amended to limit the scope of “cancer” to the types of cancers disclosed in the specification at page 2, line 4. The Examiner’s rejections are traversed below.

***Election/Restrictions and Request for Rejoinder Pursuant to MPEP 821.04***

The Examiner has made her four-way restriction requirement final in view of the serious burden imposed on the Examiner to search all of the four invention groups together. But, the Examiner has noted that she has withdrawn the lack of unity requirement based on the IPER of the corresponding PCT Application No. PCT/EP02/11353, yet the four-way restriction has been made final. However, upon telephone call by the undersigned to the Examiner on April 29, 2005 it was revealed that this conclusion was in error. But the undersigned requested the Examiner to reconsider the restriction requirement especially in view of the fact that the fragmentation of the claim scope based on Markush groups within a claim results in a massive number of permutations and combinations of divisional applications. The Examiner was open to this suggestion. The undersigned appreciates the courtesies extended by the Examiner. However, as already discussed above, Applicants have significantly amended claims 1-18 almost along the lines suggested by the Examiner in her Office Action in order to expedite the prosecution of this case. Nevertheless, since the Examiner has indicated that claims 6-17 drawn to the elected invention are in condition for allowance, Applicants respectfully request the Examiner to reconsider and broaden the scope of the elected matter simply as to the definition of R<sub>2</sub> as discussed during the teleconference.

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Further, as also discussed with the Examiner, since claim 18 depends directly upon claim 1 incorporating all of the limitations of claim 1, which further recites use thereof, it is respectfully submitted that claim 18 be rejoined pursuant to MPEP 821.04. In addition, as also suggested by the Examiner and as discussed above, Applicants have amended claim 18 to limit the scope of cancer to the types disclosed in the specification. Finally, Applicants reserve the right to place the withdrawn scope of original claims 1-18 in one or more divisional applications.

***Rejection Under 35 U.S.C. § 102(b)***

Claims 1-5 and 10 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Loewe, et al. (U. S. Pat. No. 3,996,368 (1976)).

In particular, the Examiner notes that Loewe discloses compounds in claim 1 that anticipate the instantly claimed genus wherein A is phenyl and R<sub>1</sub> is halogen and R<sub>2</sub> is -CO-alkoxy. However, claims 1-4, as amended, do not recite R<sub>1</sub> as halogen. Further, claim 5 has been canceled and claim 10 never included halogen within the definition of R<sub>1</sub>, thus obviating this rejection. In view of this, it is respectfully submitted that claims 1-4 and 10 are not anticipated by Loewe. Thus, withdrawal of this rejection as to claims 1-5 and 10 is respectfully requested.

***Rejection Under 35 U.S.C. § 112, First Paragraph***

Claim 1 stands rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Specifically, the Examiner alleges that the claim contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. More specifically, the Examiner alleges that the terms "optionally substituted," "hetero," "heteroalkyl," heteroaryl," "heterocyclylamino,"

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"heteroaryl-amino," "heterocycloalkyl," "heterocyclyl" "heteroatoms," and "prodrug" are not defined in the specification or claims.

However, Applicants respectfully disagree with the Examiner's conclusion. As noted already above, several of the objected terms have either been deleted or find support in the specification as clearly pointed out above and further discussed below. First of all, the terms such as "heteroalkyl," heteroaryl," "heterocyclyl-amino," "heteroaryl-amino," "heterocycloalkyl," and "prodrug" have been deleted, even though almost all of these terms find support in the specification. Support for "heterocyclyl" can be found broadly at page 5, lines 12 and 13 and at various places of the specification especially through specific examples as already discussed above. The definition of "heteroatoms" is also found at page 5, lines 14 and 15. Most importantly, all of these terms are routinely used in the art of medicinal chemistry, and therefore, it is submitted that one of ordinary skill in the art of medicinal chemistry readily appreciates the intended meaning of these terms. As to the use of term "optionally substituted" please note that this term is used in the specification as "eventually substituted," see at various places on page 3 of the specification, e.g., lines 8, 10, 14, 20, etc., and also on page 4. It is respectfully submitted that this is a translational error from the original French application and was specifically meant for "optionally substituted." In view of the foregoing it is respectfully submitted that claim 1, as amended, fully satisfy the requirements of 35 U.S.C. 112, first paragraph, and therefore, withdrawal of this rejection as to claim 1 is requested.

#### *Claim Objections*

Claims 6, 8, 10, 12, 13, 15 and 17 stand objected to as being dependent upon a rejected base claim.

However, as noted above, claim 1, as amended, is in condition for immediate allowance. Furthermore, claims 6, 8, 10, 12, 13, 15 and 17 depend directly or indirectly

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upon claim 1 incorporating all of the limitations of claim 1, and further recite additional limitations, thus obviating this objection. In view of this, withdrawal of objection as to claims 6, 8, 10, 12, 13, 15 and 17 is respectfully requested.

The Examiner also objects to the substituent "R<sub>2</sub>" of claim 1, page 145, line 6 because of the usage of the phrase "with the proviso that." Instead, the Examiner suggests to replace this phrase with "wherein." Applicants have considered this suggestion and have deleted the above noted phrase. However, Applicants believe that there is no need to replace with "wherein" as it is already present at line 3, page 145 of claim 1. Thus, it is respectfully submitted that objection as to claim 1 be withdrawn.

Finally, claims 7, 9 (in part), 11 (in part), 14 (in part), and 16 (in part) stand objected as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

However, again as discussed above, the base claim 1, as amended, is in condition for allowance. Further, all of objected claims 7, 9, 11, 14 and 16 depend directly or indirectly upon claim 1 incorporating all of the limitations of claim 1, and further recite additional limitations, thus obviating this objection. In addition, claims 11 and 14 have been amended to delete a few of the compounds which are no longer within the scope of amended claim 1. However, please note that all of the compounds listed in claims 9 and 16 are fully within the scope of amended claim 1 and are thus fully supported by claim 1, as amended. Thus, in view of the foregoing it is respectfully requested that objection as to claims 7, 9, 11, 14 and 16 be withdrawn.

### ***Conclusions***

In view of the above Remarks, it is respectfully submitted that claims 1-4 and 6-18 are now in condition for allowance and the early issuance of this case is respectfully

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requested. In the event the Examiner wishes to contact the undersigned regarding any matter, please call (collect if necessary) the telephone number listed below.

Applicants believe there are no fees due for this Rule 111 Amendment. However, if the Examiner deems that fees are due, please charge these fees to Deposit Account No. 18-1982 for Aventis Pharmaceuticals Inc. Bridgewater, NJ. Please credit any overpayment to Deposit Account No. 18-1982.

Respectfully submitted,

*May 12, 2005*

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